

## **AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **LISTING OF CLAIMS:**

1. to 54. (Canceled)
55. (Previously Presented) A method for identifying a compound that modulates animalia tRNA splicing endonuclease activity, the method comprising:
- (a) contacting a compound or a member of a library of compounds with an animalia tRNA splicing endonuclease and a substrate for tRNA splicing endonuclease, wherein the substrate is a nucleic acid and the nucleic acid comprises a tRNA intron within a bulge-helix-bulge structure or a mature domain of a precursor tRNA; and
  - (b) detecting the amount of substrate cleaved, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the amount of substrate cleaved in the presence of the compound is altered relative to the amount of substrate cleaved in the absence of the compound or in the presence of a negative control.
56. (Previously Presented) The method of claim 55, wherein a compound that reduces animalia tRNA splicing endonuclease activity is identified if the amount of substrate cleaved is decreased in the presence of the compound relative to the amount of substrate cleaved in the absence of the compound or the presence of a negative control.
57. (Previously Presented) The method of claim 55, wherein a compound that increases animalia tRNA splicing endonuclease activity is identified if the amount of substrate cleaved is increased in the presence of the compound relative to the amount of substrate cleaved in the absence of the compound or the presence of a negative control.
58. (Previously Presented) The method of claim 55, wherein the nucleic acid comprises a reporter gene and the tRNA intron within a bulge-helix-bulge

structure or a mature domain of a precursor tRNA is contained within the reporter gene.

59. (Previously Presented) The method of claim 58, wherein the method comprises:
- (a) contacting a compound or a member of a library of compounds with an animalia cell containing the animalia tRNA splicing endonuclease and the substrate; and
  - (b) detecting the amount of substrate cleaved by detecting the expression of the reporter gene, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or in the presence of a negative control.
60. (Previously Presented) The method of claim 58, wherein the method comprises:
- (a) contacting a compound or a member of a library of compounds with a animalia cell-free extract containing the animalia tRNA splicing endonuclease and the substrate; and
  - (b) detecting the amount of substrate cleaved by detecting the expression of the reporter gene, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or in the presence of a negative control.
61. (Previously Presented) The method of claim 59 or 60, wherein a compound that reduces animalia tRNA splicing endonuclease activity is identified if the expression of the protein encoded by the reporter gene is decreased in the presence of the compound relative to the expression of the protein in the absence of the compound or the presence of a negative control.
62. (Previously Presented) The method of claim 59 or 60, wherein a compound that increases animalia tRNA splicing endonuclease activity is identified if the expression of the protein encoded by the reporter gene is increased in the

presence of the compound relative to the expression of the protein in the absence of the compound or the presence of a negative control.

63. (Previously Presented) The method of claim 55, wherein the nucleic acid is labeled at the 5' end with a fluorophore and at the 3' end with a quencher, or the nucleic acid is labeled at the 5' end with a quencher and at the 3' end with a fluorophore.
64. (Previously Presented) The method of claim 63, wherein the method comprises:
  - (a) contacting a compound or a member of a library of compounds with an animalia cell-free extract containing the animalia tRNA splicing endonuclease and the substrate; and
  - (b) detecting the amount of substrate cleaved by measuring the fluorescence of the substrate, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the fluorescence of the substrate in the presence of the compound is altered relative to the fluorescence of the substrate in the absence of the compound or in the presence of a negative control.
65. (Previously Presented) The method of claim 63, wherein the method comprises:
  - (a) contacting a compound or a member of a library of compounds with a purified form of the animalia tRNA splicing endonuclease and the substrate; and
  - (b) detecting the amount of substrate cleaved by measuring the fluorescence of the substrate, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the fluorescence of the substrate in the presence of the compound is altered relative to the fluorescence of the substrate in the absence of the compound or in the presence of a negative control.
66. (Previously Presented) The method of claim 63, wherein the method comprises:

- (a) contacting a compound or a member of a library of compounds with an animalia cell containing the animalia tRNA splicing endonuclease substrate and the substrate; and
  - (b) detecting the amount of substrate cleaved by measuring the fluorescence of the substrate, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the fluorescence of the substrate in the presence of the compound is altered relative to the fluorescence of the substrate in the absence of the compound or in the presence of a negative control.
67. (Previously Presented) The method of claim 64, 65 or 66, wherein a compound that reduces animalia tRNA splicing endonuclease activity is identified if the fluorescent signal produced by the substrate is less detectable in the presence of the compound than the fluorescent signal produced in the absence of the compound or in the presence of a negative control.
68. (Previously Presented) The method of claim 64, 65 or 66, wherein a compound that increases animalia tRNA splicing endonuclease activity is identified if the fluorescent signal produced by the substrate is more detectable in the presence of the compound than the fluorescent signal produced in the absence of the compound or in the presence of a negative control.
69. (Previously Presented) The method of claim 55, wherein the nucleic acid is labeled at the 5' end with a fluorescent donor moiety and labeled at the 3' end with a fluorescent acceptor moiety, or the nucleic acid is labeled at the 5' end with a fluorescent acceptor moiety and labeled at the 3' end with a fluorescent donor moiety.
70. (Previously Presented) The method of claim 69, wherein the method comprises:
- (a) contacting a compound or a member of a library of compounds with an animalia cell-free extract containing the animalia tRNA splicing endonuclease and the substrate; and

- (b) detecting the amount of substrate cleaved by measuring the fluorescence of the substrate, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the fluorescence of the substrate in the presence of the compound is altered relative to the fluorescence of the substrate in the absence of the compound or in the presence of a negative control.
71. (Previously Presented) The method of claim 69, wherein the method comprises:
- (a) contacting a compound or a member of a library of compounds with a purified form of the animalia tRNA splicing endonuclease and the substrate; and
  - (b) detecting the amount of substrate cleaved by measuring the fluorescence of the substrate, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the fluorescence of the substrate in the presence of the compound is altered relative to the fluorescence of the substrate in the absence of the compound or in the presence of a negative control.
72. (Previously Presented) The method of claim 69, wherein the method comprises:
- (a) contacting a compound or a member of a library of compounds with an animalia cell containing the animalia tRNA splicing endonuclease and the substrate; and
  - (b) detecting the amount of substrate cleaved by measuring the fluorescence of the substrate, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the fluorescence of the substrate in the presence of the compound is altered relative to the fluorescence of the substrate in the absence of the compound or in the presence of a negative control.
73. (Previously Presented) The method of claim 70, 71 or 72, wherein a compound that reduces animalia tRNA splicing endonuclease activity is identified if the fluorescence emission of the fluorescent acceptor moiety at

the wavelength of the fluorescent donor moiety in the presence of the compound is increased relative to the fluorescence emission in the absence of the compound or the presence of a negative control.

74. (Previously Presented) The method of claim 70, 71 or 72, wherein a compound that increases fungal tRNA splicing endonuclease activity is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is decreased relative to the fluorescence emission in the absence of the compound or the presence of a negative control.
75. (Previously Presented) The method of claim 58, 59 or 60, wherein the reporter gene encodes at least one member of the group consisting of firefly luciferase, renilla luciferase, click beetle luciferase, green fluorescent protein, yellow fluorescent protein, red fluorescent protein, cyan fluorescent protein, blue fluorescent protein, beta-galactosidase, beta-glucoronidase, beta-lactamase, chloramphenicol acetyltransferase, and alkaline phosphatase.
76. (Previously Presented) The method of claim 59, 66 or 72, wherein the animalia cell is a human cell.
77. (Previously Presented) The method of claim 60, 64 or 70, wherein the animalia cell-free extract is a human cell-free extract.
78. (Currently Amended) The method of any one of claims 55, 58 to 60 ~~61~~, 63 to 66, or 69 to 72, wherein the animalia tRNA splicing endonuclease is a human tRNA splicing endonuclease.
79. (Previously Presented) The method of claim 56, wherein the animalia tRNA splicing endonuclease is a human tRNA splicing endonuclease.
80. (Previously Presented) The method of claim 61, wherein the animalia tRNA splicing endonuclease is a human tRNA splicing endonuclease.
81. (Previously Presented) The method of claim 67, wherein the animalia tRNA splicing endonuclease is a human tRNA splicing endonuclease.

82. (Previously Presented) The method of claim 73, wherein the animalia tRNA splicing endonuclease is a human tRNA splicing endonuclease.
83. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a subject in need thereof a compound identified according to the method of claim 56, or pharmaceutically acceptable salt thereof.
84. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a subject in need thereof a compound identified according to the method of claim 61, or pharmaceutically acceptable salt thereof.
85. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a subject in need thereof a compound identified according to the method of claim 67, or pharmaceutically acceptable salt thereof.
86. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a subject in need thereof a compound identified according to the method of claim 73, or pharmaceutically acceptable salt thereof.
87. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a human subject in need thereof a compound identified by the method of claim 79, or pharmaceutically acceptable salt thereof.
88. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a human subject in need thereof a compound identified by the method of claim 80, or pharmaceutically acceptable salt thereof.
89. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a human subject in need thereof a compound identified by the method of claim 81, or pharmaceutically acceptable salt thereof.

90. (Previously Presented) A method for treating, preventing, managing or ameliorating cancer or one or more symptoms thereof, comprising administering to a human subject in need thereof a compound identified by the method of claim 82, or pharmaceutically acceptable salt thereof.